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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,407	11/08/2006	Stephan Nees	LNK-038	5484

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SMITH PATENT CONSULTING, LLC
3307 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
SAUCIER, SANDRA E	
ART UNIT	**PAPER NUMBER**
1651	

NOTIFICATION DATE	DELIVERY MODE
09/30/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

chalin@smithpatent.com

Office Action Summary	Application No.	Applicant(s)	
	10/560,407	NEES ET AL.	
	Examiner	Art Unit	
	Sandra Saucier	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,12-22,24-37 and 39-51* is/are pending in the application.

4a) Of the above claim(s) *2, 6-10, 14-19, 24-37, 39-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5,12,13 and 20-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 December 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/2/077*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-10, 12-22, 24-37, 39-51 are pending. Claims 1, 3-5, 12, 13, 20-22 are considered on the merits. Claims 2, 6-10, 14-19, 24-37, 39-51 are withdrawn from consideration as being drawn to a non-elected invention.

Election/Restriction

Applicant's election with traverse of Group II, drawn to a method for preserving the endothelium of hollow organs that utilizes a composition comprising:
(a) a physiological electrolyte solution,
(b) a homologous anti-coagulatory-acting blood plasma preparation,
(c) a nutrient substrate in claims 1, 3-5, 12, 13, 20-22 in the reply filed on 5/509 is acknowledged.

The traversal is on the ground that the restriction is improper and that the species election is unduly restrictive. Because the prior art found by the examiner is applicable to all the species of organs, the species election has been withdrawn.

The argument concerning the impropriety of the restriction requirement is not persuasive because applicant has at least three distinct solutions disclosed in the specification in methods of use of the solutions, one of which is a plasma derived preparation (elected) while the other two appear to be synthetic solutions to which various components are added, as well as apparatus claims. These are clearly distinct because a reference which would anticipate or make obvious the use of one solution, for example, the plasma derived preparation, would not necessarily anticipate or make obvious the synthetic solutions use. Also, for example, composition A may not be restricted from compositions A+B, or from A+B+C, or from A+B+C+D as these form a tree of further limitations. However, compositions A+B and A+C and A+D, etc. are distinct compositions and may be properly restricted. Applicant has amended the claims for examination and it is appreciated.

The requirement for the species election of type of hollow organ is removed. Claims 20-22 have been fully examined.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

Claims 1, 3-5, 12, 13, 20-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There is little description of how to make the plasma preparation used in the method now under examination, which is itemized as (ii) in claim 1 and has been elected for examination. There is merely a general description of what might take place in the production of the plasma derived preparation.

Plasma is a complex liquid with many diverse proteins, including albumin, various globulins, α, β, Υ, insulin, transferrin, enzymes, such as lactate dehydrogenase, alkaline phosphatase, aspartate aminotransferase, hormones, smaller molecules such as ionic sodium, potassium, magnesium, phosphate, calcium, potassium, copper, iron, chloride, other small molecules such as glucose, amino acids, urea, bilirubin, uric acid and many other constituents. See Krebs [U2] where in 1950, around 100 components of native human plasma are known and quantitated.

The plasma preparation exemplified in Examples 9, 11 and 12 solution 4, is derived from plasma as the starting material and is also a complex liquid with, it is reasonable to assume, far more in it than the few components recited in the claims. This is because plasma, which is the starting material is extremely complex in composition.

In order to be enabling disclosure of how to make a product, either a product composition must be completely described in terms of the chemical identity of each component and the concentrations thereof OR the process of making the product must be completely described. The complete description may be either in the specification or in another document which is referenced in the specification. Neither of these situations is present in the as filed specification.

The process for making the composition used in the claimed method is not sufficiently disclosed in the specification. The multiple steps which are suggested as preferences on page 27 and 28, are sparse guidance because they lack any detail for making the apparently novel plasma preparation used in a process of maintaining viable organs. For example, conditions for anion chromatography have not been disclosed, only that DEAE Sephadex should be used. It is to be noted that there seem to be more than one variety of DEAE Sephadex, A25 and A50, and that no conditions of elution, *i.e.* the eluting solvent, temperature, duration have been revealed. A subsequent treatment with Aerosil® is mentioned, but no conditions for this treatment have been revealed. There are many kinds of Aerosil®, 12 grades of hydrophilic fumed silica, 12 grades of hydrophobic fumed silica, 3 grades of fumed mixed oxides, more than 11 grades of hydrophobic silicas and hydrophobic metal oxides, etc., all of which are called Aerosil® see [U], catalog page for Aerosil®. No teaching of which one of these diverse products which are all called Aerosil® or how to use these products to obtain applicant's specific plasma derived product used in the examples is given in the specification. Ultrafiltration and diafiltration are mentioned as being performed, but no mention of what the solvent composition used in the process should be.

There is no citation in the specification to a published paper or a patent publication which details the making of this product. Thus, the product is apparently a novel one since there is no nexus to the disclosure of prior art publications.

Another manner in which the specification can be enabling is to describe the components of a composition in detail so that a synthetic composition might be compounded from its individual components. However, the product has not been sufficiently described in detail as to its components and the concentrations thereof. For example is there antithrombin III, complement C3 or transferrin in the product and at what concentrations are these components in the plasma preparation used in the method of perfusion treatments in examples 9, 11, and 12 solution 4. Since the starting material, plasma, contains these components and many more, it may be, but it is not certain that the final composition also contains these components unless they have been removed during processing the native plasma. This disclosure is also missing from the inadequately described method of making the plasma-derived composition.

In order for a complex product such as a plasma derivative to be used in a biological method of perfusing organs to preserve or repair them for their disclosed use in grafting and transplantation, the product must be disclosed in sufficient detail in order to permit those of skill in the art to replicate it and therefore successfully practice the exemplified methods of use of that product. Preservation of organs, cells and tissues of sufficient quality for use in grafting/transplantation, which is the disclosed utility of the claimed invention is an art which to this date is not predictable. Many have tried to preserve organs with more or less success. This field is highly unpredictable and still in early experimental stages, see review by El-Wahsh [V] which reviews progress to date in formulating preservation solutions for graft preservation of the liver. See the review by Steen [W] which reviews progress in preserving the endothelium during cardiovascular surgery. Thus, it is unknown if some further components of serum, not listed in the specification, also have the salutary effects on the organ's preservation which is exemplified in the specification. The unlisted component's effects on preservation may not be fully appreciated at this time.

If applicants have made an advance in this important and unpredictable medical field, it is incumbent upon them to fully disclose how they have made the advance in preservation solutions for organs. This they have not done.

An enabling description of how to make this apparently novel product, which is used in the perfusion method of the claims, is critical and is missing from the disclosure. It is considered that the specification is fatally flawed in this respect.

INDEFINITE

Claims 1, 3-5, 12, 13, 20-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 uses the term "unstable components", but fails to state what these components are or how they are to be determined. Unstable is a term of comparison without any definition of what might be encompassed by this term. All components of plasma will be unstable, i.e. degraded if left for periods of time under at least some conditions of temperature, oxygen exposure, light etc..

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:A person shall be entitled to a patent unless(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action: (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-5, 12, 20-22 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over US 4,073,886 [A] or US 3,998,946 [B].

The claims are directed to a method of contacting an isolated hollow organ with a perfusion solution comprising:
a) physiological electrolyte solution,
b) a homologous, anti-coagulatory blood plasma preparation comprising human plasma proteins, anti-coagulatory acting factors and immunoglobulins from which the procoagulatory acting factors, isoagglutinins and unstable components of the blood plasma have been removed,
c) a nutrient substrate.

The references are relied upon as explained below.

US 4,073,886 disclose a treated plasma preparation for use as an organ (specifically mentioned kidney, heart, lung) perfusate where the coagulation factors have been removed. The plasma preparation is citrated and sterile, Example 1. A plasma derived preparation such as disclosed would be reasonably assumed to have physiological electrolytes and nutrients in it because plasma has these components.

US 3,998,946 disclose a treated plasma preparation where plasminogen-plasmin system, fibrinogin, lipoproteins have been removed used for organ perfusion such as kidney. Immunoglobulin concentration is not changed (col. 5, l. 43). The product is sterile. A plasma derived preparation such as disclosed would be reasonably assumed to have physiological electrolytes and nutrients in it because plasma has these components.

With regard to the components recited in claim 4, all of these components are considered to be present in the compositions of the prior art references in the absence of evidence to the contrary, because they are all present in the starting material, plasma.

Likewise the concentrations of the components recited in claims 5, 12 are considered to be the same as or so close to, that in the absence of evidence to the contrary, they are not patentably distinguishable from the inherent concentrations of these substances in the cited prior art plasma preparations.

With regard to the differences in concentrations between the instant claims and the disclosure of the prior art, see MPEP 2144.05 I. and II.

Generally differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation, *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

To establish unexpected results over a claimed range, applicants should compare a sufficient number of tests both inside and outside the claimed range to show the criticality of the claimed range. *In re Hill*, 284 F.2d 955 (CCPA 1960). MPEP 716.02(d).

With regard to the type of hollow organ, *i.e.* specifically blood vessels, the references both generically disclose that the plasma preparations disclosed in the references may be used to perfuse organs. The generic term "organs" includes all organs and therefore, encompasses blood vessels and lymphatic vessels. Therefore it would be obvious to employ the plasma preparations of the cited prior art for blood vessels, lymphatic vessels or any other organ in the absence of evidence of criticality.

Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over4,073,886 [A] or US 3,998,946 [B] as applied to claims 1, 3-5, 12, 20-22 above, and further in view of Dichtelmuller *et al.* [X].

The claims are further directed to the use of a β-propiolactone, UV treated plasma preparation.

Dichtelmuller *et al*. teach a process of treating plasma and plasma derivatives with β-propiolactone and UV irradiation in order to inactivate viruses present in the plasma or plasma derivative (Summary, p. 367)

One of ordinary skill in the art would have been motivated at the time of invention to make these additions in order to obtain the results as suggested by the references with a reasonable expectation of success. The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

Conclusion

Applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06). It is applicants' burden to indicate how amendments are supported by the ORIGINAL disclosure. Due to the procedure outlined in MPEP 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 USC 102 or 35 USC 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending applications that set forth similar subject matter to the present claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Saucier whose telephone number is (571) 272-0922. The examiner can normally be reached on Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, M. Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Sandra Saucier/
Primary Examiner, Art Unit 1651